IN BRIEF

HIV

A higher hurdle to eliminate HIV?

Although antiretroviral therapy does not eradicate latent HIV that resides in resting T cells, efforts are underway to determine how this latent HIV can be awakened. However, Ho *et al.* showed that the latent reservoir might be much larger — up to 60-fold — than previously estimated. The authors analysed non-induced proviral clones from patients treated with antiviral therapy and showed that over 10% had intact genomes and were capable of being transcriptionally active. The authors note this means that these viruses might become active *in vivo*, thus increasing the barrier that needs to be overcome to cure HIV.

ORIGINAL RESEARCH PAPER Ho,Y-. C. *et al.* Replication-competent noninduced proviruses in the latent reservoir increase barrier to HIV-1 cure. *Cell* **155**, 540–551 (2013)

OBESITY AND DIABETES

Mitochondrial uncoupler blocks metabolic disease

This paper investigated whether metabolic disease could be improved by mitochondrial uncoupling agents that oxidize hepatic triglyceride. To this end, the authors studied a liver-targeted, methyl ether derivative of 2,4-dinitrophenol; the parent compound is a known weight loss agent but it also induces fatal hyperthermia. In rats that were fed a high-fat diet, the derivative reversed hypertriglyceridaemia, fatty liver disease and insulin resistance, and it decreased hyperglycaemia in a rat model of diabetes. Importantly, hepatic and systemic toxicities were not observed and the derivative did not induce hyperthermia.

ORIGINAL RESEARCH PAPER Perry, R. J. *et al.* Reversal of hypertriglyceridemia, fatty liver disease, and insulin resistance by a liver-targeted mitochondrial uncoupler. *Cell Metab.* **18**, 740–748 (2013)

PHARMACOGENOMICS

Divergence in drug data between studies

This study analysed data from two recent large-scale pharmacogenomic studies: the Cancer Genome Project and the Cancer Cell line Encyclopedia. Overlapping data from these studies (15 drugs and 471 cell lines were tested in both studies) enabled the authors to show that genomic data were well correlated between studies, but the drug response data were very divergent. The authors note that this creates an obstacle to the use of data from individual studies to make or validate predictive models of drug response.

ORIGINAL RESEARCH PAPER Haibe-Kains, B. *et al.* Inconsistency in large pharmacogenomic studies. *Nature* http://dx.doi.org/10.1038/nature12831 (2013)

NANOTECHNOLOGY

RNAi-based nanoparticles zap glioblastoma

Several oncogenes are known to be involved in glioblastoma multiforme pathogenesis but no therapies are currently available. Jensen *et al.* evaluated an RNA interference spherical nucleic acid (RNAi–SNA) nanoparticle conjugate to neutralize oncogene expression in a mouse model of glioblastoma. Systemically delivered SNAs that targeted the oncoprotein BCL2-like protein 12 — which could penetrate the blood–brain barrier and blood–tumour barrier — increased intratumoral apoptosis and reduced tumour burden and progression. This suggests that silencing anti-apoptotic signalling using RNAi–SNAs could be a new approach for brain tumour therapy.

ORIGINAL RESEARCH PAPER Jensen, S. A. *et al.* Spherical nucleic acid nanoparticle conjugates as an RNAi-based therapy for glioblastoma. *Sci. Transl. Med.* **5**, 209ra152 (2013)